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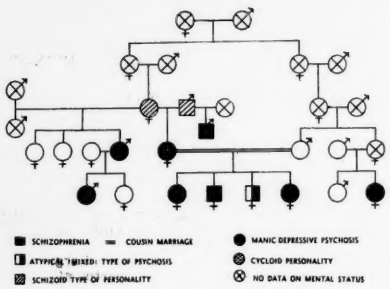

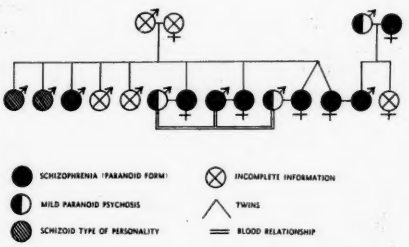

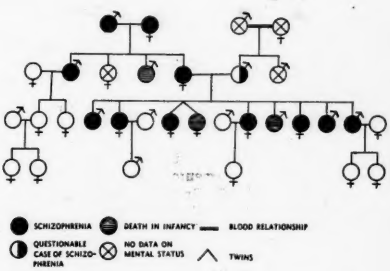

SCHIZOGENETICS OR INFECTIOUS INSANTY?
(SEE PAGE 298)

Changing Sex Mechanisms in Platyfish

Quintuplet Calves With the Same Blood Mosaic

VOLUME 37 OCTOBER, 1946 NUMBER 10

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The JOURNAL OF HEREDITY is published monthly by the AMERICAN GENETIC ASSOCIATION at 32nd Street and Elm Avenue, Baltimore, Md., and 1507 M St., N. W., Washington, D. C. Address all communications regarding editorial matters to 1507 M. St., N. W., Washington, D. C. Communications regarding the business management of THE JOURNAL OF HEREDITY may be addressed to the publication office, 32nd Street and Elm Avenue, Baltimore, Md., or to 1507 M St., N. W., Washington 5, D. C. Entered as second-class matter February 24, 1923, at the postoffice at Baltimore, Maryland. Acceptance for mailing at the special rate of postage provided for in section 1103, Act of October 3, 1917, authorized December 29, 1918.

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The

Journal of Heredity

Vol. XXXVII **OCTOBER, 1946** **No. 10**

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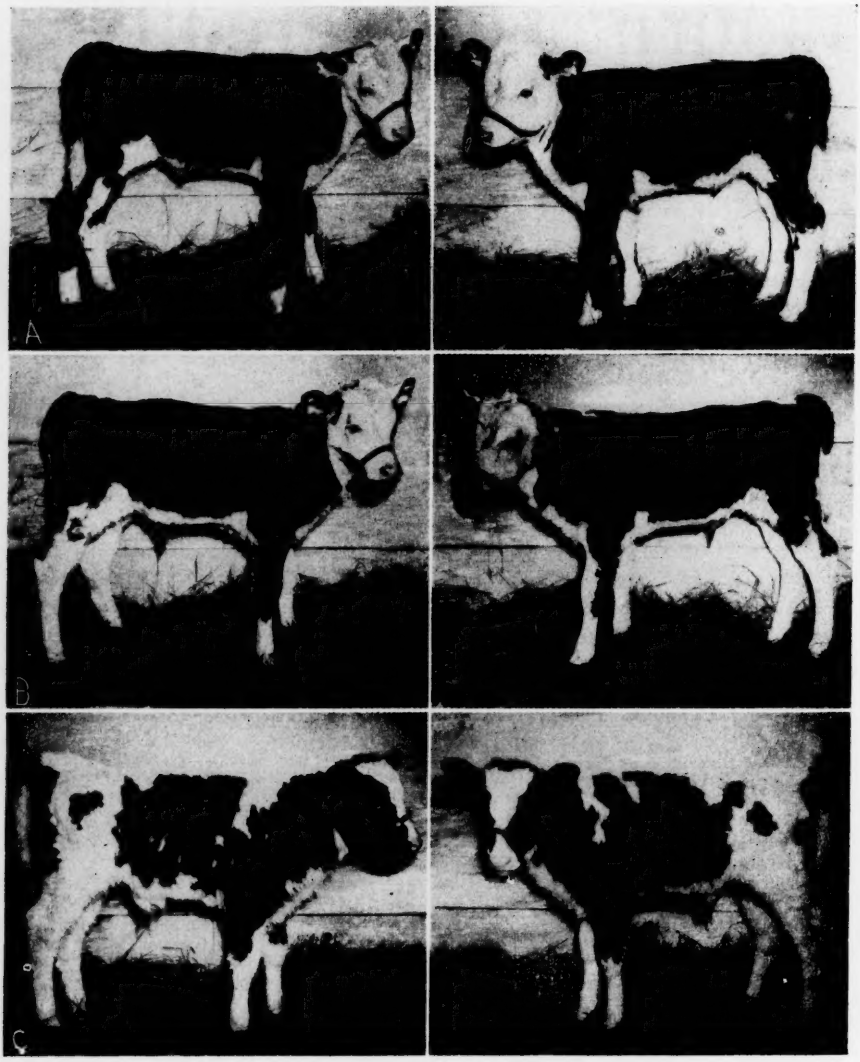


SAME BLOOD-ANTIGENS BUT DIFFERENT GENOTYPES

Figure 1

Right and left sides of *United States* (*A*), *Russia* (*B*), and *China* (*C*), the three cattle quints having spotted coats. All three are males, and all have the same blood antigen complex, as have all five of the quints. In coat-pattern, *United States* and *Russia* show definite similarity, but on other grounds it is considered unlikely that they are identical.

QUINTUPLET CALVES AND ERYTHROCYTE MOSAICISM*

R. D. Owen, H. P. Davis and R. F. Morgan

At about nine o'clock on the morning of November 20, 1945, a red cow called *Old Glory* was turned out to pasture on the farm of Leo B. Schmoldt, Route 1, Fairbury, Nebraska. About 3:30 P. M., Mr. Schmoldt noticed that a calf—later to be known as *United States*—had been born. Mr. Schmoldt went back to the house to get a small truck, and upon his return found a second calf—*England*. The calves were put into the truck and their dam followed them to the barn.

Turning from his chores at about 4:30 P. M., Mr. Schmoldt found a third calf —*Russia*. He bedded down the manger in front of the cow and put the three calves in the manger. But *Old Glory* wasn't finished; at about 5:15 P. M., *China* appeared, and at 6:00, *France*, the last to arrive and the only heifer in the group. The calves were given colostrum, using the "finger in the pan" technique, that night.

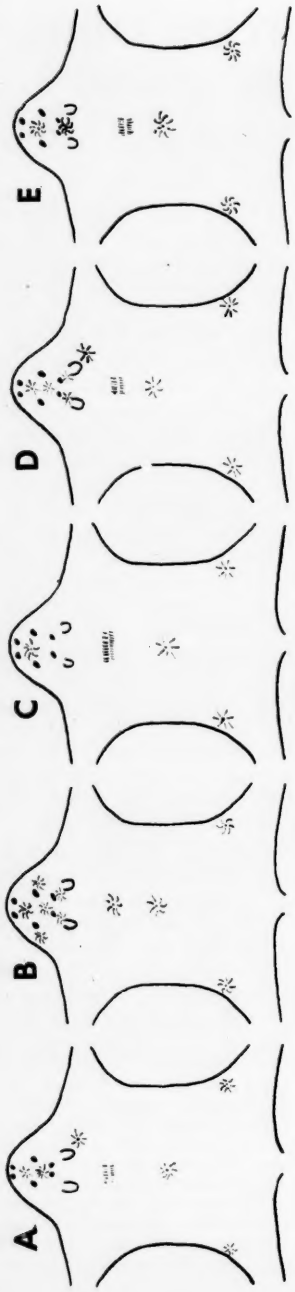
Shortly afterward, through the cooperation of the Fairbury Chamber of Commerce, a separate building, heated by electric brooders, was erected to house the quintuplets. They were fed four times daily with whole milk from a bottle, and were given rolled oats and a little "calf starter" to nibble on. Dr. L. J. Smith (who has been called the "Dr. Dafoe" of the case) and his wife gave the calves almost constant care; he and Mr. Schmoldt devoted most of one day to helping in the collection of the data included in this paper. Dr. Smith drew the blood samples for the tests reported here.

Old Glory and the Big Five

Old Glory (Figure 4*A*) is a grade polled Shorthorn, believed to be seven years old. She was raised on Mr. Schmoldt's farm, and has had three calves, each a single birth, previous to her *opus major*. Little is known of her pedigree, but Mr. Schmoldt recalls that her dam, a polled red Shorthorn with some white on the underline, had one set of twins. No breeding records have been kept, but a Hereford bull (Figure 4*B*) had been running with the herd for 287 days before the birth of the quintuplets, and his "blood type" as well as the appearance of the calves, are consistent with the assumption that he is their sire. His predecessor in the pasture was a roan Shorthorn bull, that left the pasture about two or three weeks before the Hereford arrived there.

Old Glory failed to discharge the quintuplet afterbirth. Part of it was removed after flushing, the day after the calves were born. After being flushed on three successive days the dam suffered a uterine hemorrhage. It was not possible to determine with certainty the number or character of the fetal envelopes.

*Joint contribution from the Departments of Genetics (Paper No. 355) and Zoology, Univ. of Wisconsin, and the Dairy Husbandry Department, Univ. of Nebraska. The authors acknowledge their indebtedness to Mr. H. Livingston of the First National Bank of Fairbury for his help in arranging for this study, and to Mrs. Mary W. Yeas in connection with the blood tests and cell counts. The aspect of this study dealing with cellular antigens is part of a program in cooperation with the Bureau of Animal Industry, U. S. Department of Agriculture, and is aided by grants from the American Guernsey Cattle Club, the Holstein-Friesian Association of America, and the Rockefeller Foundation. The authors are Assistant Professor of Genetics and Zoology, The University of Wisconsin; Professor and Chairman of the Dairy Husbandry Dept., The University of Nebraska; and Assistant Professor of Dairy Husbandry, The University of Nebraska, respectively.



HAIR-WHORL PATTERNS
Figure 2
A—United States; B—Russia; C—China; D—England; E—France.

An examination of photographs of the quintuplets (Figures 1 and 3) suggests that they originated from at least four fertilized eggs. *France* and *England* are almost self brownish-red; *England* has a white tip to his tail while *France* has a white spot under her right flank. Only the right sides of these animals are pictured. *China* is marked with broken white spotting, while *United States* and *Russia* show Hereford markings. Both sides of the latter three are shown in the photographs. The pigmented areas in the coats of all five calves are brownish red. The similarity of the white markings of *United States* and *Russia* is superficially striking, but detailed comparison shows that they differ in certain details and are no more similar than are many animals with the dominant white spotting of the Hereford. The sire is symmetrical in his marking. It appears that he is heterozygous for the Hereford white-spotting factor.

Hair-whorl patterns show considerable variation among the calves (Figure 2). It will be noted that *United States* and *Russia,* similar though they be in white markings, differ greatly in number, location and character of hair whorls. There is some indication in the literature[3] that close similarity in hair-whorl patterns (or mirror-imaging) is one of several consequences of genetic identity in twin cattle. The contrast between *United States* and *Russia* in this characteristic, as well as their difference in horn buttons, to be mentioned below, together with Mr. Schmoldt's expressed belief that there were five placental "sacks," and the generally accepted low frequency of identical twinning in cattle, combine to indicate that these quintuplets are all fraternal. One other point in favor of the conclusion that they represent five different fertilized eggs is their birth order. *United States* and *Russia* were the first and third calves born; *England* appeared between them. Hutt[2] has pointed out that in plural births of this sort, identical calves might be expected to be born consecutively.

Thus the only pair in this set of quintuplets whose color markings are at all consistent with the hypothesis that they are identical, are probably excluded as identicals by the weight of other evidence.

Weights and Measurements

Weights of the quintuplets are presented in Table I. It will be noted that the four bulls started out nearly equal in weight; and that, except for *China's* relative decline on the last weighing, their growth has followed a very uniform course. *France*, the heifer, was somewhat lighter than the bulls three days after birth, but her weight has shown increments comparable to those of her brothers, again excepting *China's* defection at the last weighing. The first weights on these calves may be compared, roughly, with the mean birth weight of 77.1 pounds for Shorthorn male × Hereford female crossbreds.[1] Each quintuplet was apparently a little less than half as heavy as a normal single calf at birth; the combined weights of the quintuplets was more than twice as great as that of the average single calf. Their growth since birth has been approximately normal relative to their birth weight.

Various standard measurements of the quintuplets are summarized in Table II. The data are uniform, the homogeneity within the group extending even to *France*, whose consistently lower weight is not to be explained as a consequence of a smaller frame.

Certain additional, qualitative comparisons are made in Table III. Noteworthy points include the protruding incisors of *France;* the fact that only *Russia* lacked horn buttons on the date indicated, and the differences in nose color. As would indeed be expected, *France* shows early indications of freemartinism; she has a protruding, infantile vagina and her clitoris is long and stiff, resembling a penis. She urinates to the left side. She has four small teats and no indication of testicles.

Table I.—Weights of Quintuplets

Date of Weighing	Weight in Pounds				
	United States	*England*	*Russia*	*China*	*France*
11-23-45	37.5	37.0	38.0	37.5	32.0
11-30-45	38.0	37.0	39.0	39.0	33.0
12-7-45	42.0	43.0	43.0	43.0	37.0
12-14-45	44.0	44.0	44.0	45.0	41.0
12-22-45	55.0	55.0	55.0	54.0	49.0
1-13-46	75.5	78.5	75.5	68.5	70.5

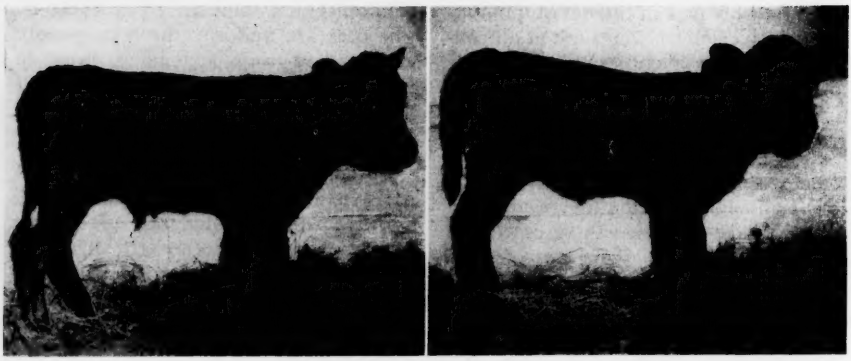
TABLE II.—Measurements in Centimeters (January 16, 1946)

Measurement	*United States*	*England*	*Russia*	*China*	*France*
Length of body					
Tape	57.0	58.0	58.0	57.0	57.0
Calp.	54.5	56.0	55.5	55.0	55.0
Length of top line	36.0	36.0	37.0	35.0	36.0
Length of Rump					
Tape	22.5	24.0	23.0	22.0	23.0
Calp.	22.0	23.0	22.5	22.0	22.5
Girth					
Barrel	83.0	85.0	84.0	80.0	82.0
Heart	79.0	80.0	78.0	76.0	78.0
Height					
Withers	67.0	68.5	66.0	66.0	67.0
Hooks	67.5	72.0	67.5	67.5	70.0
Pins	67.5	69.0	67.5	67.0	68.0
Diagonal length	68.5	71.0	69.0	66.0	66.5
Depth					
Barrel	27.0	29.0	27.5	28.0	28.0
Chest	27.0	28.0	28.0	27.0	27.5
Width					
Chest	16.5	17.5	17.5	15.5	16.5
Hooks	17.0	17.5	17.0	15.5	16.5
Pins	11.0	10.5	11.5	10.0	10.5
Thickness of hide					
Fore flank	0.4	0.35	0.4	0.4	0.45
Last rib	0.4	0.4	0.45	0.45	0.48

TABLE III.—Other Comparisons of the Quintuplets (January 16, 1946)

Characteristics	*United States*	*England*	*Russia*	*China*	*France*
Number of incisors	8	8	8	8	8*
Horn buttons	normal	normal	none indicated	normal	normal
Nose	flesh color	darker	flesh color	flesh color	smoky
Testicles	normal	normal	normal	normal	none

*Lower incisors protrude past upper jaw.



ENGLAND AND FRANCE

Figure 3

Both calves are the same color of brownish-red. *England* (*A*) has a white tail-tip and *France* has a white spot under her flank. Association with four brothers during embryonic life has modified *France's* blood antigen pattern and her sex differentiation, so that she will probably develop into a freemartin.

Tests for Inherited Cellular Antigens

Tests of the bloods of the quintuplets and their presumed sire and dam are summarized in Table IV. Reagents for forty inherited cellular antigens, not all of which have been described in publications, were used in this analysis. Only antigens present in one or more of the bloods are listed in the table.*

It will be noted that these animals have relatively few of the cellular antigens segregating in cattle; the seven animals together possess only fourteen of the forty antigens now identified. Furthermore, the sire and dam are similar in "blood type," being alike in nine of the blood characters (*A, C, E, F,* O_2, O_3, *Y, C',* and *H'* and different in only five (*H,* X_2, *D', E'*$_3$, and *I'*). Except for antigen *F,* for which there is adequate serological evidence that these animals are all homozygous,† there is no way at present of distinguishing heterozygous from homozygous animals in this series.

Two of the antigens found in the parents, *H* (in the probable sire) and X_2 (in the dam), are absent from the quintuplets' bloods. The remaining twelve antigens found in either the sire's blood or the dam's, or both, are present in all five calves. The quintuplets are therefore identical in gross blood type. This apparent identity may be surprising in view of the conclusion reached above that at least four, and very probably five, separate fertilized eggs are represented by the quintuplets. It might be formally explained by the legitimate assumption that one or both of the parents are homozygous for certain of the genes controlling their cellular characteristics, as they both certainly are for *F,* and by a further recourse to random sampling from heterozygous parents. It is of course in general highly improbable that five animals not genetically identical would have the same blood types. Fur-

TABLE IV.—Blood Types

Sire	A C EF H	O_2O_3	YC'D' H'I'
Dam—*Old Glory*	A C EF	O_2O_3	X_2YC' E'$_3$H'
United States	A C EF	O_2O_3	YC'D'E'$_3$H'I'
England	A C EF	O_2O_3	YC'D'E'$_3$H'I'
Russia	A C EF	O_2O_3	YC'D'E'$_3$H'I'
China	A C EF	O_2O_3	YC'D'E'$_3$H'I'
France	A C EF	O_2O_3	YC'D'E'$_3$H'I'

*For a description of these tests and citations of prior references see Stormont and Cumley.[6]

†The basis for this statement is unpublished work primarily by C. Stormont, on the *F* antigen.

PROUD PARENTS

Figure 4

A—Old Glory, mother of the bovine *Big Five* quintuplets (Figures 1 and 3). The Hereford bull (*B*) is the putative father, with a roan Shorthorn bull in second place as bovine Papa Dionne. However, the blood-type evidence strongly supports the Hereford's claims to this honor.

thermore, it will be demonstrated below that the true explanation for the apparent identity of blood types among the quintuplets lies in another quarter.

Differential Lysis

Tests on several thousand animals have shown that the blood cells of practically all individuals possessing *A* antigen are completely lysed by the "*A*-reagent" under the standard test conditions. In other words, all the blood cells of such animals have *A*, and are susceptible to lysis by the "*A*-reagant" in the presence of complement. Thus all the blood cells of both the dam and the sire of the quintuplets were destroyed by the "*A*-reagent" in the tests. But cell suspensions from each of the quintuplets were only partially lysed by the "*A*-reagent" under test conditions; a fraction of the erythrocytes of each quintuplet was unaffected. These results suggest that some of the erythrocytes of each calf have *A*, and the remainder of them lack this antigen.

Similarly, although all the blood cells of normal animals having *C* and *E* are regularly lysed by the "*CE*-reagent," test cell suspensions from each of the quintuplets were only partially lysed by this reagent. Cells reclaimed after treatment with the "*A*-reagent," and unaffected by it, were all lysed when tested with the "*CE*-reagent," and cells unaffected by the "*CE*-reagent" could be completely lysed by the "*A*-reagent." These observations indicate that the blood cell population of each quintuplet is a mosaic of at least two distinct types of cells: those having *A* without *CE*, and those having *CE* without *A*. No cells lacking both of these antigens are present in any of the calves. Direct demonstration of the remaining possible combination, *A CE*, could not be accomplished with the technique of differential lysis.

An estimate of the relative proportions of *A* and "non-*A*" cells in each quintuplet can be derived from the cell-counts summarized in Table V.

TABLE V.—Blood Cell Counts in Test Suspensions

Name	Cells per unit volume* of test suspension			
	Control	After lysis with "*A*-reagent"	Per cent cells lacking *A*	Per cent cells having *A*
United States	433	69	15.9	84.1
England	479	77.6	16.2	83.8
Russia	523	80.5	15.4	84.6
China	348	51	14.7	85.3
France	350	52	14.8	85.2

*Averages of actual counts of cells in 0.004 cu. mm. of test suspension.

In order to control the lytic tests, one drop of the test suspension was mixed with two drops of physiological saline and one drop of complement. At the same time, a parallel series was set up, using the same test suspensions and complement, but substituting two drops of the standard, diluted "*A*-reagent" for the saline. The cell-counts were made after the "*A*-reagent," in the "treated" series, had been allowed sufficient time to destroy all cells having the *A* antigen. There was, of course, no lysis in the controls. It should be emphasized that these counts represent cells per unit volume (actually 0.004 cu. mm.) of washed test suspension, and they cannot without considerable error be converted back to figures representative of the total cell-count in the whole blood of the quintuplets. They suit their purpose of comparison here, however, since these data are concerned not with the total number of cells per c.c. in the whole blood of the quintuplets, but with the relative number of *A* and "non-*A*" cells in test suspensions taken from these bloods. Each figure in the table represents the average of a number of independent counts.

It will be noted that, although the number of cells per unit volume varies considerably from one test suspension to another, the percentage of cells unaffected by the reagent is remarkably uniform for the five animals. These results indicate that the blood-cell-population of each quintuplet is a mosaic, about 15% of the cells of each animal lacking *A* and 85% of the cells of each animal having this antigen. It was impossible at this time to make similar cell-counts after treatment with the *CE* reagent; however, both the original tests and the results of differential lysis with this reagent were entirely compatible with the conclusions drawn above relative to *A* and "non-*A*" cells.

Discussion

Erythrocyte mosaicism comparable to that encountered here, associated with multiple births in cattle, has been suggested in previous publications.[4,5] Briefly, it appears to involve an intermixture of two or more genetically and phenotypically distinct types of blood cells, consequent upon the intermingling of fetal bloods through the vascular anastomoses commonly associated with multiple pregnancies in cattle. The permanence of blood types so modified has indicated that embryonal cells, ancestral to the erythrocytes of the animal, are exchanged by the embryos and become established in the hemapoietic tissues of the co-twins, quadruplets or quintuplets, continuing to provide sources of blood cells distinct from those of their host throughout his life.

The homogeneity of these quintuplets, with respect to their relative proportions of *A* and "non-*A*" cells, indicates a very thorough intermixture of at least two different cell-types among the quintuplets as embryos. Assuming from the cell-counts that one of these five calves may be genetically "non-*A*," and that each of the other four may have inherited the factor for *A* antigen from one or both of his parents, the evidence indicates that the circulating "non-*A*" cells were distributed equally to all five embryos, and that the cellular progeny of *A* and "non-*A*" cells have maintained practically constant numerical relationships in all five hosts. There is no way of concluding, from the tests, which of the quintuplets was the original "non-*A*" zygote, and therefore no indication here that the predominant cell-type of an individual in a case of this sort is the type consistent with the individual's own genotype. In short, these data suggest that most or all of the erythrocytes of cattle descend from cells originally circulating in the embryo, and that cells having a "local origin" within the hemapoietic tissues of the individual do not contribute significantly to the population of mature erythrocytes.

The description by Hutt[2] of a set of bovine quadruplets illustrates in another way the same thorough and intimate intermixture of bloods. These quadruplets included one bull and three heifers. To quote Hutt, ". . . one bull calf produced enough testicular hormone to affect seriously the reproductive systems

of the three females, but although there were apparently vascular connections between the bull and all three heifers, the combined endocrine secretions of the latter were unable to affect the reproductive system of the bull." Whatever the present status or future prospects of the hormonal explanation of freemartinism, there can be little doubt that Hutt's observation indicates thorough intermixture of bloods of the four embryos through vascular anastomosis, just as the present study depends on the same phenomenon to explain the identical blood types of quintuplets.

Summary

Descriptive data on a set of living bovine quintuplets, one modified heifer and four bulls, suggest that the animals developed from five different fertilized eggs. Their bloods, however, gave identical results when tested for inherited cellular antigens. This result is consistent with the conclusions: (1) that placental anastomoses had given all five embryos a common circulation; (2) that wholesale exchange and intermixture of circulating cells among the embryos was therefore effected; and (3) that the exchanged cells became established in the hemapoietic tissues of the five animals, so that the circulating erythrocytes, the cellular descendants of these exchanged elements, now represent a genetic mosaic, similar in all of the quintuplets.

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HETEROCYCLICITY OR POLYSOMATY?

To The Editor:

My researches on somatic doubling, and a study of the recent literature suggest another interpretation of Prokofieva-Belgovskaja's findings reported in the August 1946 issue.

Prokofieva's Figure 12,* like Meurman's[8] Figures 3 and 11, seems to be too accurately reproduced to support the interpretation she has placed upon it. In the figures in question, the manifestly paired association of many of the chromosomes (indicated by our encirclement of the most obvious cases in a reproduction of Prokofieva's Figure 12—see page 306) points to the interpretation that she has illustrated a case of polysomaty.

Comparatively recently the investigations of Berger,[1] Ervin,[2] Gentcheff and Gustafsson,[3] Langlet,[4] de Litardière,[6] Lorz[7] *et. al.* have pointed out that cells having multiples of the normal somatic number of chromosomes are of common, if not universal, occurrence in the Angiospermae. While there may be minor points of disagreement among these investigators, all are in substantial agreement that the paired association of the chromosomes in polysomatic cells is indicative of the recent occurrence of a double chromosomal reproduction in antecedent mitotic stages. When our thinking conforms to the more modern concept of the reproduction of the ultimate longitudinal chromosomal constituents by a synthesis of a new 'daughter' chain of molecules alongside of the old 'mother' chain, then in the paired associations encountered in polysomaty the individual pairs should be composed of one mother and one daughter chromosome. If a kind of heteropycnotic difference exists between mother and daughter chromosomes then such a difference should be manifest between the two members of a pair since the paired association is an indication that all mother chromosomes do not collect in one part of the cell and the daughter chromosomes in another, as the heteropycnotic difference expressed in Prokofieva's Figure 12 suggests. This consideration should shed some light on the perplexity expressed by Muller with regard to the grouping of mother and daughter chromosomes.† Although, at present, no alternative suggests itself to account for the heteropycnotic difference between the right and left halves of the figure depicted by Prokofieva, her theory seems inadequate to cope with the evidence from the paired association of many of the chromosomes that this is simply a polysomatic cell.

(*Continued on page* 306)

**Jour. Hered.* August 1946: "Mother" and "Daughter" Chromosomes. †Same issue: Comment by H. J. Muller.

GENETIC CONCEPTS AND FOLIE À DEUX

A Reexamination of "Induced Insanity" in Family Units*

By Franz J. Kallmann and Jean S. Mickey†

AMERICAN psychiatry enters its second century of existence and growth with a record of immense scientific headway achieved in a relatively short time. The practical results of this progress have been remarkable on all fronts. Modern psychiatry has taken its proper place as a guardian of public mental health. However, some primordial misconceptions still manage to survive. Of these, one of the most anachronous and loosely defined is the concept of induced insanity, called *folie à deux,* or psychosis of association.

The French term *folie à deux* which literally means "insanity of two", has been more popular than any of its numerous translated substitutes. The original and still widely accepted definition of the term was given by Lasègue and Falret in 1877, but there had been earlier references to the same condition under such synonyms as infectious insanity (Ideler, 1838), psychic contagion (Hofbauer, 1846) and delirious mental infection (Baillarger, 1857). Other synonymous expressions have been collective, contagious, simultaneous, reciprocal or double insanity, mystic paranoia, and induced, influenced, imposed, communicated or associated psychosis. The various terms used in distinguishing the active and passive partners of a *"folie à deux"* combination were recently collected by Gralnick.

According to the old definition of Lasègue and Falret, *folie à deux* is the transference of delusional ideas from a psychotic individual to intimate associates who have been under his domineering influence for a long time, and it may be extended to three or more persons (*folie à trois, à quartre,* etc.). Although the possible significance of inheritance was vaguely recognized in familial cases of *folie à deux,* no clear distinction was made between consanguineous members of family units and those who were unrelated by blood. It should be remembered, however, that the original formulation of the concept antedated by a few decades Kraepelin's description of dementia praecox (1893) and the rediscovery of Mendel's law (1900).

In its broadest and more recent connotation, the concept of *folie à deux* has been indiscriminately applied to the coexistence of any mental disorders of a similar variety in two or more persons who were deemed closely enough associated. The term has been used to describe the occurrence of various psychotic syndromes in entire sibships or other family units. It has been used to explain the coincidence of similar schizophrenic or manic-depressive symptoms in twin pairs, regardless of whether or not the twin partners lived together when they developed their psychoses. One of the most recently published twin cases described as *"folie à deux"* was that of two monozygotic twin sisters of 52, who showed similar paranoid syndromes of schizophrenic origin although they had been separated at the age of nine months.[7] In the opinion of some writers, the term has even served to prove that "all mental illness is man's active response to disturbed human relationships," irrespective of heredity.

This "sociogenetic" concept has been

*Read at the Inter-hospital Conference in Syracuse, April 23, 1946.

†From the Department of Medical Genetics of the New York State Psychiatric Institute and Hospital, New York 32, N. Y.

blended with a few new-fashioned versions of the long discredited theories of Darwin, Spencer and Lamarck about pangenesis and the inheritance of acquired characteristics. The result has been an almost superstitious belief in a mysterious phenomenon that produces mental disease through personal contact. In this rather nebulous manner, *folie à deux* has been stretched into a convenient cover for investigators who continue to be opposed to the principle of human heredity in any form.

In order to justify such sweeping extensions of the old but clearly definable concept of *folie à deux*, it would be necessary to disprove the validity of some of the most elemental theories of modern human genetics and the statistics of chance distribution. Besides, it ought to be possible to state in fairly precise terms how intimate a contact between persons should be, and how distorted their relationship, if a real "psychosis of association" is to emerge. Whenever such a psychosis fails to develop despite the prevalence of definitely "inductive" circumstances, one should be able to determine by which protective device the given persons managed to withstand the pressure of their psychotic contacts.

Furthermore, if a schizophrenic mother should happen to transfer her paranoid delusions to only one of five daughters, her association with the delusional daughter should prove to have been closer than with the others. Moreover, her domineering influence upon the family should be shown to have been less pronounced than that of any mother who, "by personal contact", implanted her schizophrenic symptoms into all of her children. If this concept of *folie à deux* is true it should certainly *not* be possible to match every family history, in which a delusional mother apparently induced her mentally normal children, "to follow her into schizophrenic unreality", with just as many other histories in which an equally psychotic mother had no "distorting" effect upon her offspring, or in which a schizophrenic patient developed a similar symptomatology without any psychotic associates.

In the interpretation of such histories it would seem advisable to consider the possibility that disintegrated family relationships might as well be the effect as the cause of two or more psychotic personalities in that unit. For obvious reasons, it is in the nature of the family system in our culture that the closest relatives tend to share the same environment more often than they do not. Therefore, a convincing explanation should be found for those many instances, in which members of dilapidated family units, with or without accumulation of actively psychotic cases, either show no mental deviation whatsoever or develop psychotic syndromes of a completely different variety.

A few family histories, taken from our series of psychotic twin index families, may serve to illustrate that there is no consistent relationship between the social disintegration of a particular family background and the number or type of psychotic phenomena developed by the different members of such family units.

THE A. FAMILY

The *A. family* presents a picture which might be called *folie à neuf*—similar schizophrenic symptoms in two parents and seven of their children (Figure 5). The remaining two children of this union died as infants, including a twin.

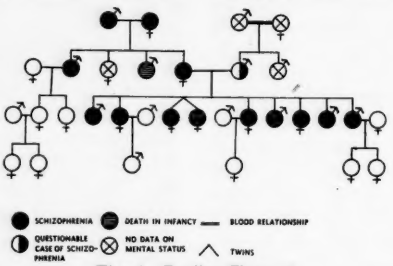
The mother had her first mental breakdown while in high school. Following her third childbirth at the age of 26, she developed a slowly progressive schizophrenic psychosis as had apparently been true for both of her parents. Her predominantly catatonic process was characterized by delusions, hallucinations and frequent states of agitated confusion, and remained essentially uncontrolled, leading to death in a mental institution at age 53.

The father came from a prosperous Bostonian family and was the son of a cousin marriage. He failed as a shoe manufacturer and subsequently worked as a shoe cutter, farmer, night watchman and orderly. He

frequently was out of work and never provided adequate support for his family. Although he probably was hospitalized only once for a short time in his earlier life, he was described as a very peculiar, indolent and self-absorbed person, preoccupied with problems of phrenology, astrology and insanity.

The two oldest sons left the cheerless home of their parents soon after graduation from high school and had been away for a number of years when they developed delusional and hallucinatory symptoms. One was a married and well-established mechanic and the other was in the navy. On admission to different institutions, both had ideas of poisoning and persecution in a basically catatonic syndrome with negativistic stupor, incoherent speech and stereotyped movements.

Of the four daughters, only one was married, but no one of the others was living at home when they began to show schizophrenic symptoms of different varieties. Two of them were committed to a reformatory because of illegitimate pregnancies and a tendency to promiscuity. Their symptomatology was typically hebephrenic—with silliness, persistent giggling and bizarre delusions—and soon resulted in marked deterioration. The married daughter developed an agitated, paranoid psychosis following a Caesarian operation at age 23 and died a few years later of tuberculosis. The youngest daughter was fifteen years old when her mother died, and supported herself as a secretary for about five years before she became listless, confused and actively hallucinated. She saw her father walking around in the yard and heard peculiar references to her mother over the radio. Following elopement with a male patient of the same hospital, she deteriorated rapidly and died of an abdominal disorder at the home of another man who had promised to marry her.



The A. Family—Figure 5

The remaining son was the pet of the family and received the careful treatment of a favorite child. He was not informed about the mental disorders of the older siblings and, at the age of 11, was sent away from home to attend a farm and trade school. When he was about to graduate he showed signs of a serious personality change and had to be hospitalized for over a year. He was apprehensive, childish, and bewildered, complained about electric sensations in his body, and heard strange persons accusing him over the radio. Following his discharge, he married an elderly widow and worked for a while in a navy yard. His present behavior is so peculiar that he may soon have to be rehospitalized.

Comment

It would probably be difficult to find a kinship disclosing either a more complete dissolution of its family interrelationships or a greater variety of schizophrenic syndromes than that reported in the A. family. Since all adult members of this unit showed some kind of delusional tendency, one might think of classifying their mental condition as *"folie à neuf."* However, it seems inadequate to explain their entire psychopathology on the basis of family disintegration or some other aspect of their unfavorable social background. A glance at the pedigree might indicate the possibility that it was not without significance for the distribution of schizophrenia in the various sibships of the A. family whether a schizophrenic parent was married to a schizophrenic or a non-schizophrenic mate.

THE S. FAMILY

The social setting of the *S. family* (Figure 6) was equally disturbed and intermingled, but it gave rise to an accumulation of atypical psychoses in only seven of its eight members. One might say that it led to the development of *"folie à sept."*

The father of this interesting sibship of six was a moody, ill-tempered and querulous tailor in a small New England town. He had more dependents than customers and terrorized all of them. At the age of 53, following an especially fiery argument with his wife, he went to his store, locked doors and windows, and turned on the gas. He was revived by the police, but remained a demented miser and invalid until he died in a mental hospital about 11 years later.

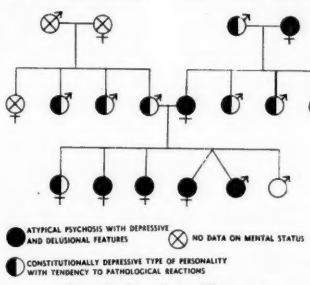
The mother had been restless and depressed at the time of her marriage at age 28, but she evidently did her best to take care of her large family and the husband's tailoring business. Following his suicidal attempt and the onset of their oldest daughter's psychosis, she developed an agitated depression with delusional ideas of reference and guilt. Her condition required hospitalization for almost four years and was classified as involutional melancholia. Since her discharge in 1941, she has been moderately depressed and suspicious, but she is now free of acute delusional symp-

toms. In her attitude toward the children, her outstanding weakness has been a tendency to timid overprotection rather than coercion.

In addition to the parents, the maternal family record includes an unstable and overscrupulous grandfather and an apparently manic-depressive grandmother with ten hospital admissions. No information is available about the paternal ancestry.

Of the four daughters, the two oldest are extremely sensitive, timid and easily discouraged. They have a history of many depressive brooding spells with obsessive fears and delusional ideas of guilt. One of them had to be hospitalized in 1937 when she was disturbed by the thought that she had been responsible for her father's illness and the kidnapping of the Lindbergh baby. Her anxiety state was diagnosed as obsessional neurosis.

The third single-born daughter required ambulatory psychiatric treatment from 1937 to 1942, and five months of hospitalization (Psychiatric Institute) in 1945. She had always been restless, fearful and discontented, had very few friends, and never worked steadily. On admission she showed a bewildered and dejected attitude with compulsive and hypochondriacal complaints, psychomotor retardation and ideas of reference, but gave no evidence of hallucinations. She improved considerably following insulin treatment, although she remained inadequate in her general adjustment and self-control. Her acute psychotic episode was diagnosed as schizophrenia, catatonic type.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ATYPICAL PSYCHOSIS WITH DEPRESSIVE AND DELUSIONAL FEATURES
NO DATA ON MENTAL STATUS
CONSTITUTIONALLY DEPRESSIVE TYPE OF PERSONALITY WITH TENDENCY TO PATHOLOGICAL REACTIONS

The S. Family*—Figure 6

The behavior of the twin daughter, Sophie, presented no major problems until age 22, when she was confronted with an accumulation of adverse circumstances. She was engaged to marry. Her fiancé wanted to be married soon, while her family wanted her to take care of the mother who was due to be paroled from the hospital. She had withheld the story of her mother's illness from her fiancé and was now afraid of losing him as well as her job in exchange for the enforced loyalty to her family. She became listless and depressed, developed an obsessional fear of insanity, and one night attempted to drink iodine. In the hospital she appeared agitated and dejected and, after a few weeks, began to express somatic delusions in connection with a transitory experience resembling an acute hallucinatory episode. She felt humiliated by a gathering of many patients who pointed their fingers at her and indicated that she was a freak. From this time on she kept covering her face with her hands and maintained the delusional idea that she was a horrible monstrosity without nose, stomach and intestines. The persistence of this state for several months led to the change of the original diagnosis of manic-depressive psychosis to that of schizophrenia, hebephrenic form. Following electric shock therapy, Sophie gradually relinquished her delusional beliefs and finally recovered. She is now married and expects a child.

Sophie's twin brother, Morris, had a very similar type of psychosis, except for a less acute onset and a more chronic course of disease. His difficulties began in high school and were attached to a sensitive resentment about his protruding "donkey ears." He attempted to paste them back, but was so afraid of being teased because of this excessive correction that he withdrew from all social activities. After he had saved some money, he had two plastic operations performed on his ears and, for a while, felt much relieved. He obtained a job, attended parties, and maintained a steadier relationship with a young girl whom he wanted to marry. Gradually he became again concerned about his ears and was obsessed by the idea that having them changed to an "unnatural" position had been a despicable act and detracted from his moral character. He was so perturbed by this thought that he urged the surgeon to perform another operation in order to restore the original state of the ears. He gave up his job and finally consented to psychiatric rather than surgical treatment.

While in the hospital, Morris responded fairly well to psychotherapy. He realized reluctantly that his delusional concern about the malposition of his ears was basically a personality problem associated with his inade-

*Because of their interesting psychotic features which resembled Kretschmer's sensitive reference psychosis, several members of this family were presented by Drs. W. Horwitz and F. J. Kallmann at a meeting of the New York Society for Clinical Psychiatry on April 9, 1942.

quacy in coping with emotional conflicts. Soon after his discharge, however, he began to make up new excuses for avoiding any active struggle with an apparently hostile world. He failed to return to work and seems now resigned to a childlike existence which is tolerated by the five female members of his family.

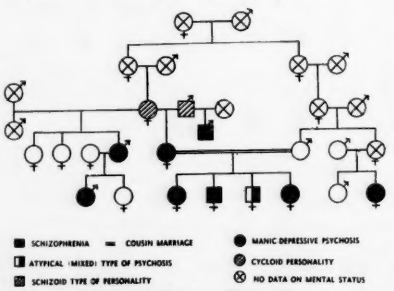
The youngest son has always been different in appearance and behavior. He is happily married, has many friends and outside interests, and shows no evidence of a pathological reaction to the unhappy family situation. There is some reason for questioning the paternity of his legal father.

Comment

Regardless of whether the similar mental deviations of this family unit are classified as atypical varieties of a schizophrenic or manic-depressive psychosis or as unusual forms of an obsessive anxiety state with paranoid coloring, they were distinguished by circumscribed delusions of reference in hypersensitive, unstable and physically dysplastic individuals with a limited capacity for adjustment to frustrating circumstances. There are no objections to applying the term *folie à sept* to the appearance of such a syndrome in seven closely associated family members. It should not be implied, however, that the consequent family disintegration was the primary cause, or that true schizophrenic or manic-depressive symptoms may originate by contagion or mass suggestion. It is apparent that most of the members of the S. family were constitutionally unable to establish a more prosperous and stabilized social level or to express their emotional difficulties in any other way than that of a depressive reaction syndrome with predominantly introjective trends.

THE N. FAMILY

Under particular circumstances it may happen, of course, that the same dilapidated family background becomes the matrix of two different psychotic reaction types. An example of such a coincidence is the *N. family* (Figure 7), in which a combination of true schizophrenic and manic-depressive psychoses occurred in a unit of four sisters* and their mother, providing a sample of *"folie à cinq."*



The N. Family—Figure 7

The four sisters grew up in a poverty-stricken home on New York's lower east side. Only the oldest married, but the onset of her psychosis preceded the marriage. She is a true manic-depressive, while the second had a typical schizophrenic psychosis, the third has been some kind of a mixture in between, and the fourth is also classifiable as manic-depressive.

The cyclic attacks of the oldest sister began at the age of 17 and recurred at frequent intervals, lasting from four weeks to five months. The manic states usually developed overnight without apparent precipitating causes and cleared up just as rapidly; they have been relatively short and mild since the availability of shock treatment. The depressive episodes started and disappeared more gradually and lasted longer; they were simple depressions without evidence of delusions or hallucinations. Their recurrence has been more irregular in recent years and can be broken up with shock therapy. The attacks of the youngest sister have been very similar, but they generally are of a somewhat milder variety.

The third sister was quiet and bashful as a child, although she had no difficulty in school. At age 17, she became listless, preoccupied and delusional. Two years later she was admitted to a mental hospital where she was described as dull, grimacing, resistive and actively hallucinated. She expressed many delusions, thought that other patients were influencing her mind, and felt constantly annoyed by voices of men making improper sexual approaches to her. She deteriorated rapidly and died of pulmonary tuberculosis at the age of 22.

The fourth sister was also 17 years old when she had her first depressive episode, which after two months suddenly changed to a state of elated excitement before it cleared up. Except for a few short depressions, she remained free of psychotic symptoms for over ten years. At the age of 28, while at a camp for unemployed women, she developed an acute psychosis with negativistic tenseness, mutism and confusion, which required hospitalization for almost three years. She

*Their clinical histories were presented by Drs. W. H. Horwitz and F. J. Kallmann at a meeting of the Psychiatrical Society of the Metropolitan State Hospitals held on April 7, 1941.

showed frequent changes between retarded and excited behavior, and on discharge was described as definitely disintegrated in her entire personality. On this deteriorated level, there have been several recurrences of depression and confusion, which were interrupted with different methods of shock therapy.

The mother of this sibship was married to a second cousin, an illiterate but fairly placid peddler with arrested tuberculosis. She had repeated depressive episodes, during which she lived with one of her sisters. She died at age 43, following a suicidal attempt and an operation for gall stones.

The maternal grandmother was definitely cycloid in her temperament and made an active contribution to our understanding of the concurrence of manic-depressive and schizophrenic syndromes among her descendants. She married three times, had children with each of her three husbands, and thereby disclosed that she happened to be a carrier of the predisposition to both schizophrenia and manic-depressive psychosis. The children of her subsequent two marriages included a son who was a typical manic-depressive. Her first husband, the grandfather of the four sisters, was an eccentric and seclusive minister who also remarried, providing a third group of half-siblings for the mother of the original sibship under investigation. In his second marriage he had a son, who developed schizophrenia at an early age and died in a mental institution after many years of hospitalization. The cousin marriage of the latter's half-sister apparently made it possible for her to have schizophrenic and manic-depressive daughters with the same husband.

Comment

It may be doubtful whether the combination of the two psychotic syndromes in this family unit would be called *"folie à cinq"* by any advocate of the diluted concept of induced insanity in closely associated family members. Unquestionably, however, it would be very difficult to explain their coexistence in the same disorganized unit *without* demonstrable genetic evidence of the presence of two specific predispositions. This finding may be taken as an indication that poor environment, intimate contact and suggestibility are *not* sufficient to produce an accumulation of manic-depressive or schizophrenic psychoses in certain family units. The basic factor required seems to be that of *blood relationship,* without which there is no inheritance. If it were possible to substantiate this hypothesis, there would be no point in labeling the occurrence of similar psychotic syndromes in blood relatives *"folie à deux."*

SCHIZOPHRENIA AND GENETICS

At this stage of affairs, geneticists are called upon to supply conclusive evidence to the effect that the chance of developing, for instance, a true schizophrenic psychosis in comparable environments increases in direct proportion to the degree of blood relationship to a schizophrenic index case. At the same time, supporters of purely environmental theories should be expected to demonstrate with equally precise methods that a consistent increase in socially induced schizophrenic cases of close associates is found *in the absence* of consanguinity. There seems to be no need for speculative interpretation if adequate experimental methods are available to clarify a controversial and evidently complex problem.

We recently completed a study of the prevalence of schizophrenia in the sibships of a statistically representative sample of 691 schizophrenic twin index cases. The results of this analysis are summarized in Table I. They clearly show that the vast majority of siblings and two-egg cotwins—namely, from 90 to over 98 per cent—do *not* develop

TABLE I. Schizophrenia Rates in Schizophrenic Index Families

	Relationship to Schizophrenic Index Cases						
	General Population	Marriage Partners	Step-Siblings	Half-Siblings	Full Siblings	Two-Egg Cotwins	One-Egg Cotwins
Absence of Schizophrenia in Per Cent (Uncorrected)	99.0	98.0	98.6	95.5	89.8	89.7	31.0
Corrected Schizophrenia Rate	0.85	2.1	1.8	7.0	14.3	14.7	85.8

schizophrenia even if they share the same environment with a schizophrenic brother or sister. Despite intimate association with at least one delusional relative, all of these persons appear sufficiently protected against an induced psychosis simply by virtue of being not predisposed to a schizophrenic process. It is indicated by the statistically corrected schizophrenia rates for the various sibship groups of our index families that their variations in morbidity are consistently correlated with different degrees of consanguinity to a schizophrenic index case, but not with similarity or dissimilarity in their respective environments. About one-quarter of one-egg twin pairs show concordance as to schizophrenia without similar environment, while close to one-half of two-egg twin partners remain discordant even if they have been exposed to the same environment.*

These observations imply that the concept of *folie à deux* may be useful for the practice of counting in French, but not for describing the occurrence of similar schizophrenic symptoms in twin pairs or other units of blood relatives. The continued use of the term in family units would seem inadequate without proving specifically that it is *not* the factor of blood relationship which is primarily at work. Such a qualification should practically limit the application of the term to transference of delusional ideas in two groups of closely associated persons who are not related by blood; namely, marriage partners and intimate friends living together.

In applying the concept of induced insanity to consorts, that is, to the psychiatric features of a *conjugal psychosis* with similar delusions, one should be careful to exclude the possible effect of "mate selection". It is of interest to note that the schizophrenia rate for marriage partners of schizophrenic index cases (2.1 per cent) slightly exceeds the general population rate of 0.85 per cent (Table I). However, 98 per cent of the consorts do not develop schizophrenia, and the very small statistical difference is easily referable to the operation of factors which limit the selection of mates for actual and potential schizophrenics. The history of the *K. family* provides an illustration that may serve to illuminate this point (Figure 8).

THE K. FAMILY

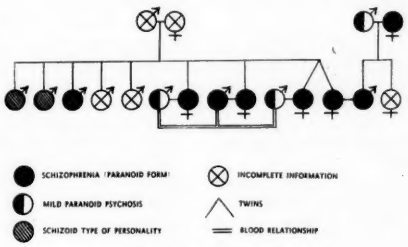
The twin sisters, Kitty and Tilly, grew up in a small town under fairly comfortable circumstances. They never looked alike and were not more attached to each other than they were to the seven other brothers and sisters. They lost both parents at a relatively young age. Of the five brothers, two died of tuberculosis in their early thirties, one married a cousin of Kitty's husband before he developed a deteriorating type of schizophrenia, and two became stingy and seclusive fanatics who never married.

The twins worked on their father's farm until their marriages to two unrelated farmers around the age of 25. From then on, they saw each other only infrequently. However, their socio-economic conditions remained approximately the same and there was considerable resemblance in the paranoid symptomatology of their schizophrenic psychoses which developed independently about ten years later. Kitty's need for prolonged hospitalization arose partly because she had no one who could take care of her at home. Her husband began to show symptoms of a depressive psychosis with delusions around the age of 50. He died a few years later in the same mental hospital to which both of his parents had been committed about twenty years before him. The diagnosis of the three in-laws was involutional melancholia; and that of Kitty, dementia praecox, paranoid type.

Tilly and her two other sisters were married to three "scions" of the same family, two brothers and a first cousin who all had their own modest farms on the fringe of civilization. There is no use in speculating which factor may have been most influential in restricting the mating choice of, or in precipitating the first delusional symptoms in, the

*The detailed findings of this study were reported at the meeting of the American Psychiatric Association in Chicago, May 27-30, 1946, and will be published in the *American Journal of Psychiatry* (Franz J. Kallmann: "The Genetic Theory of Schizophrenia").

members of which family. It is definite, however, that all the six mates developed paranoid psychoses, all of which were classifiable as schizophrenic although the personality changes of the husbands were relatively mild and required no hospitalization.



The K. Family—Figure 8

to follow him or her into a delusional world. In fact, all of the mates continued to be psychotic even following separation by hospitalization or death, and there was no evidence for the assumption that celibacy might have protected any one of them against the familial threat of a delusional psychosis. Evidently, we are dealing here with a more or less coincidental accumulation of apparently endogenous psychoses in three inbred families, which were thrown together by chance and those other circumstances beyond their own control that limited the mate selection of their descendants.

Comment

From a purely sociological standpoint it might be interesting whether this K. family would be best described as *folie à six*, or *folie à huit* or *folie à onze*. Psychiatrically there is no reason to believe, however, that one member of this family was a mysteriously domineering agitator who induced all the others by some moral pressure

Conclusions

In order to save the useful and time-honored concept of *folie à deux* from becoming a meaningless or deceptive colloquialism, it seems advisable to add another qualifying stipulation to its original and clearly delineated definition, which restricted the application of the term to the transference of circumscribed delusions in closely associated persons. The main objective of contemporary psychiatry is the understanding of psychopathologic behavior patterns in mentally ill individuals rather than description of their symptoms in speculative or ideological terms. There is no room for loosely defined or inexactly applied concepts in any branch of modern psychosomatic medicine, nor should we permit any scientific theory to stray too far from the truth.

The *additional restrictive qualification* to be advocated is that similar delusional syndromes should not be called *"induced"*, or *folie à deux*, if they appear in units of *blood relatives*, and if the primary significance of the factor of *blood relationship* cannot be safely excluded.

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✦

HETEROCYCLICITY OF POLYSOMATY?

(*Continued from page 297*)

It is not inconceivable that the binucleate cells are merely manifestations of amitoses associated with differentiation into permanent tissues and with degenerative changes which culminate in the death of the cell. Such amitoses could be responsible primarily for a quantitative difference in the two nuclei of a binucleate cell and the secondary result would be the occurrence of qualitative differences arising out of the unequal apportionment of the hereditary material.

Two other considerations are consistent with the suggestion that Prokofieva's Figure 12 represents a newly established polysomatic metaphase: 1. Polysomatic cells, although not always interpreted as such at first encounter, have been found rather characteristically in tuberous growths such as crown gall tissue in beets (Winge[9]) and in rhizobial tubercles on the roots of legumes (Wipf and Cooper[10]). 2. They are likely to be encountered in meristematically *old* tissues (i.e. tissues in which the cells have not quite lost their capacity to divide but show some degree of differentiation as evidenced by the presence of vacuoles, plastids, starch grains and other inclusions). Levine[5] pointed out that the higher multiples of the somatic chromosome number occur in the older portions of the crown gall tumor, and the literature abounds with references to the now classic case in *Spinacia* where multiples of the somatic number occur regularly in the older regions of the periblem of the root just before the cessation of meristematic activity.

In view of these considerations a reiteration of our title seems in order. Is this "heterocyclicity or polysomaty"?

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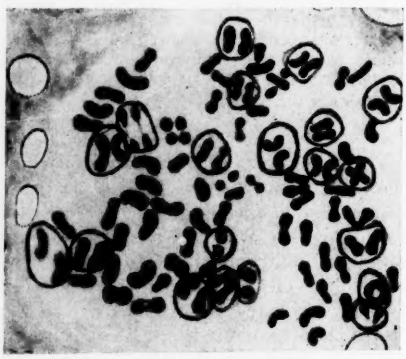

EXAMPLE OF POLYSOMATY?

Figure 8A

Nucleus of bark parenchyma cell of potato tuber showing existence of two distinct complexes of chromosomes differing in basophily. The complex of chromosomes on the right part of the nucleus are pycnotic and intensely stained. Those in the left sector are less deeply stained and not as compact. . . .

[A reproduction of part of Prokofieva's Figure 12 (*Jour. Hered* August 1946). The cases where a paired association of the chromosomes is manifest are encircled by Lorz who considers these as evidence of polysomatic origin.]

INTERCHANGING GENETIC MECHANISMS FOR SEX DETERMINATION

In Fishes Under Domestication*

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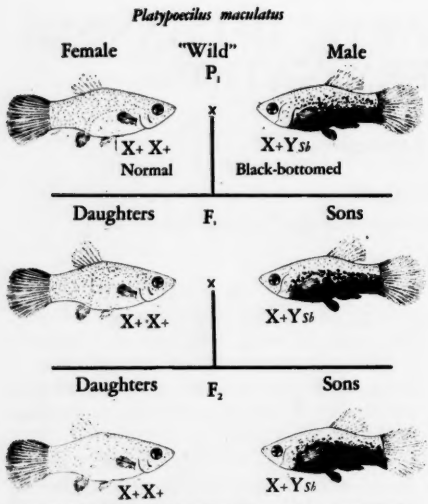
A NUMBER of divergent genetic systems have been suggested to explain the perplexingly diverse sex-determining mechanisms in the platyfish-swordtail group of fishes. The eight† or more major contributions to a solution of this enigma are considered in this paper, together with new data of the author. Upon one basic fact there seems to be universal agreement: the platyfish (*Platypoecilus maculatus*) of the common aquarium-bred stocks, has the WZ = female and ZZ = male type of genetic sex determination found in the moth *Abraxas* and in the domestic fowl. This fact was originally established by Bellamy[1] in 1922, and reaffirmed by him in his later publications. The fact that the female of this species and strain was heterogametic and the male was homogametic for sex-determining factors was confirmed independently by Gordon,[16] and supported by Fraser and Gordon[12] and by other workers.[5,28]

While the type of genetic sex-determining mechanism was clear in the aquarium-bred platyfish, it was, and still is, obscure in the swordtail (*Xiphophorus hellerii*). This is because the "wild" swordtail has no phenotypically demonstrable sex-linked factors of its own. Some authors, notably Kosswig[28] and Breider,[5] describe the actions of the swordtail genes: red body color (*R*), black body color (*N*) and montezuma pattern (*Mo*). But there are no red, black or montezuma patterned swordtails in the wild populations of this species, nor did they originate as mutants in the aquarium-bred swordtails. All of these color varieties of the swordtail are the result of introgressive hybridization with the platyfish, according to Gordon.[21,22] In other words, the color genes *R, N* and *Mo,* originally the exclusive property of the platyfish, have been bred into the aquarium swordtail.

Gordon concludes that practically all domesticated swordtails used by geneticists heretofore are swordtails reconstructed out of platyfish-swordtail hybrids; these swordtails must carry some platyfish genes or even whole chromosomes. Perhaps the hybrid nature of the "domesticated" swordtails has been responsible for the divergent results and the consequent diversity of opinion concerning the real nature of the genetic mechanism of sex-determination in swordtail-platyfish hybrids. Kosswig, for instance, calls the swordtail a latent hermaphrodite and says that its definitive sex is greatly influenced by environmental factors. Harms[25] regards the male swordtail the heterogametic sex, while Goldschmidt[13] thinks that the female swordtail is the heterogametic form. Essenberg[11] has described a case of complete and functional sex reversal in an aquarium-bred swordtail. This brief review will not attempt to add to the interpretations of the sex-determining factors in this species but, at a later

*Aided in part by grants from the Anna Fuller Fund and the American Cancer Society upon recommendation of the Committee on Growth of the National Research Council. Laboratory facilities were provided by the American Museum of Natural History. Collections made in Mexico in 1939 were made possible by the John Simon Guggenheim Memorial Foundation.

†Explanations have been presented by Breider and Kosswig,[7] Castle,[8,9] D'Ancona,[10] Goldschmidt,[13] Kosswig,[26] Rust,[31] Winge,[32] Witschi,[35] and others.



BLACK-BOTTOM SEX LINKAGE IN 1932

Figure 9

Illustrates the genetic behavior of the first and only black-bottom male platyfish caught in nature from the Rio Tonto, Oaxaca, Mexico, in 1932. When mated to a "wild" recessive female, the male's gene *Sb* was transmitted only to his sons; in the next generation a similar behavior resulted: *Sb* was transmitted from father to son. The obvious explanation that *Sb* was carried by the Y chromosome as indicated in the figure was not consistent with the sex-determining mechanism then known for *Platypoecilus maculatus* (see Figure 11).

point, an example will be given of the differential effects of the association of the "wild" swordtail (sex?) chromosomes with the sex chromosomes of the platyfish.

It is first necessary to review the evidence for the sex-determining mechanism in *Platypoecilus maculatus* in the light of the recent work on pure wild-stocks. Gordon[19] said that for over twenty years fish geneticists have repeatedly found that domesticated female platyfish are heterogametic (WZ) and the males are homogametic (ZZ) with respect to sex-linked genes. Further, Fraser and Gordon[12] showed that W-borne dominant genes are transmitted from mother to daughters. However, a "wild" population of *P. maculatus* from the Rio Jamapa at Plaza de Agua near Veracruz, Mexico, manifested the opposite type of sex-determining mechanism: wild males were heterogametic (XY) and the wild females homogametic (XX). It is obviously important, in view of this situation, to designate clearly which stocks of the common platyfish one is using, for "wild" and "domesticated" types have opposing types of sex determination.

How did the "wild" or male heterogametic type become transformed under "domestication" into the female heterogametic type? Towards the solution of this problem the case history of the spotted-belly (*Sb*) mutant of *P. maculatus* (better known as the "black-bottom" platy) will be presented.

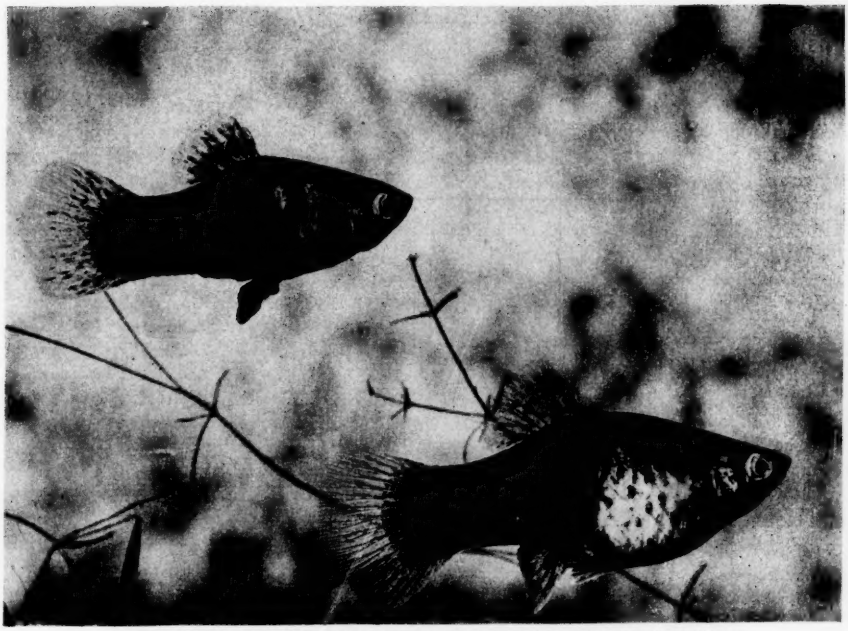
The *Sb* gene was discovered[18] in 1932 in a single member of a natural platyfish population inhabiting a jungle pool near the Rio Tonto in the State of Oaxaca, Mexico. Together with a number of other natural varieties, the spotted-belly platyfish was shipped to Ithaca, New York, where it was tested over several years in the fish-genetics laboratory at Cornell University. In 1933 a number of black-bottom platyfish were given to a fish fancier in Geneva, New York, and from there the strain spread to tropical fish hatcheries in Florida and elsewhere in the United States and Canada.

This paper, in part, is a report on the genetic behavior of the *Sb* gene under "natural" breeding conditions, under "domesticated" breeding practices of fish fanciers, and on *Sb*'s behavior when, after seven years of "domestication," the gene *Sb* was tested with "wild" genes of newly caught Mexican platyfish.

The *Sb* Gene in Wild Stock

The original black-bottom platyfish (*Sb*) was a vigorous male. When mated to normally* colored females (+), he invariably produced black-bottom

*As used in this paper the word "Normal" refers to recessiveness; it does not imply that the dominants are abnormal.



A SEX-LINKAGE ENIGMA—THE BLACK-BOTTOM PLATYFISH

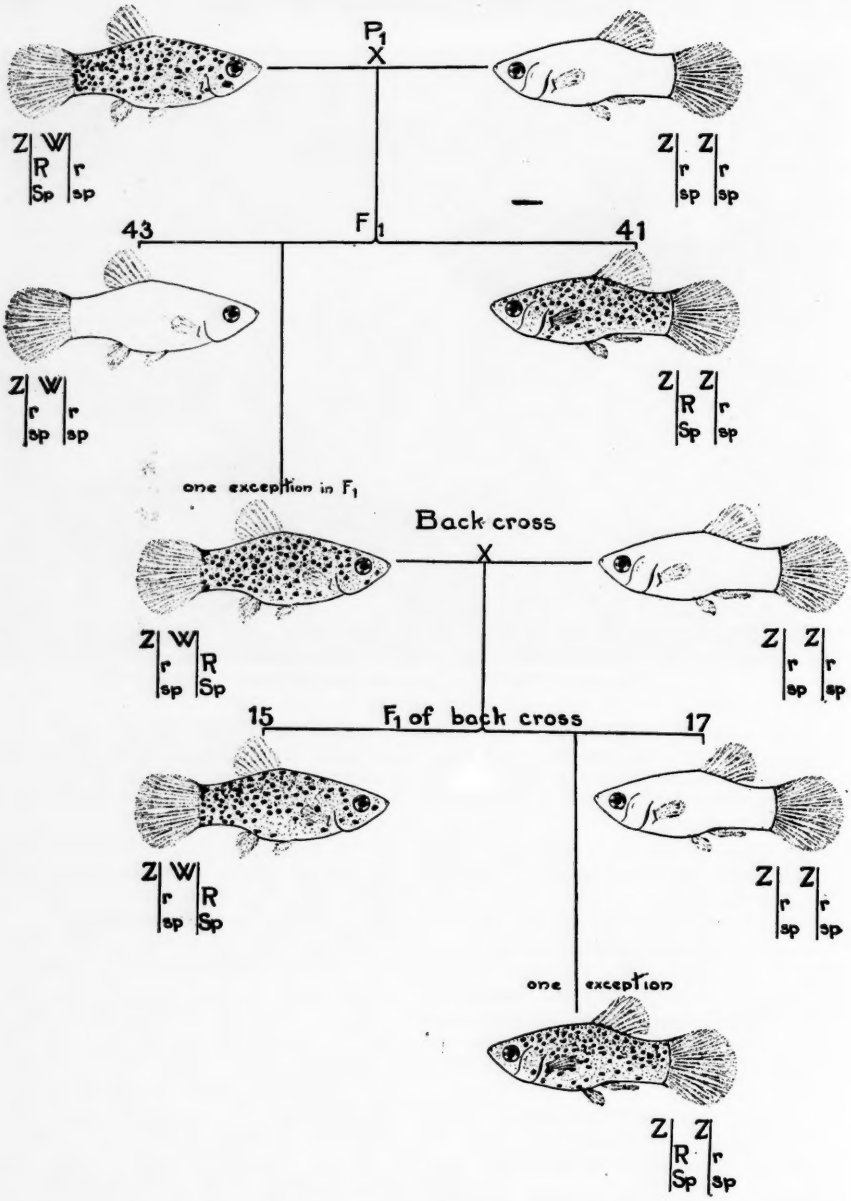
Figure 10

A single male "black-bottom" fish captured in 1932 in Mexico, was the progenitor of all aquarium platies thus patterned. During ten years under "domestication" the relation of the sex-linked gene conditioning the pattern shifted in an unprecedented manner. An understanding of this anomalous behavior may throw new light on the evolution of sex-determining mechanisms.

sons (*Sb*) of which in one experiment there were 15, and normally colored daughters (+) of which there were 20. (See Figure 9). When the F_1's were inbred, the normally colored mothers produced 29 black-bottomed sons and 27 recessive, normally colored daughters. The "father-to-son" type of inheritance was clearly evident again and this was repeated in the production of the third generation.

Now, if these experiments using *Platypoecilus maculatus* had been the first of their kind to have been performed, the father-to-son reactions would have been easy to explain, for they were much like the results that Winge obtained in his *Lebistes* crosses. Winge[32, 33] found a number of genes that were inherited through the Y chromosome of the male guppy fish. Some of the sex-linked genes crossed over to the X, but others remained firmly associated with the Y to give the unfailing father-to-son type of inheritance.

Hesitation in accepting, in 1932-1933, the *Lebistes* explanation for *Platypoecilus* rested on the knowledge that Bellamy,[1, 2] Gordon,[14] Fraser and Gordon,[12] and Kosswig[26] all agreed from their independent genetic work that *Platypoecilus maculatus* had the type of the sex-determining chromosomal mechanism opposite to that of *Lebistes*. *Lebistes* had the *Drosophila* type (XY-male, XX-female), whereas *Platypoecilus* had the *Abraxas* type (ZZ-male, WZ-female). Thus the results obtained from the black-bottom male did not conform to the established genetic behavior of the platyfish as then known (Figure 11). The possibility that the genetic behavior



THE MECHANISM OF SEX DETERMINATION IN PLATYPOECILUS MACULATUS AS IT WAS KNOWN IN 1932

Figure 11

(*Legend on page* 311)

of the "wild" was in opposition to the "domesticated" platyfish did not seem plausible.

Other Wild Sex-Linked Genes

In 1939 another expedition to Mexico afforded new data. Over 8,000 platyfish were caught from the Rio Papaloapan and the Rio Jamapa. A representative sample of the many color varieties was shipped alive to the New York Aquarium laboratory while many platyfish were preserved for studies of distribution of gene frequencies.[21] After careful inspection of each specimen it was found that the black-bottomed variety was not represented in the 1939 populations of either of these river systems.

Three varieties with scattered black markings were found among the wild stock of the platyfish from the Rio Jamapa. It was discovered by experiment that three patterns could be referred to sex-linked genes: an irregularly spotted variety (gene = *Sp*); a variety in which the spots produced a striped effect (gene = *Sr*); a variety in which the spots were restricted to the dorsal fin (*Sd*). Full details of the genetic experiments with these three sex-linked genes will be published elsewhere,[23] but one of the matings involving all three is illustrated in Figure 12. The experiment shown in this diagram, and others of like nature, clearly demonstrates the fact that "wild" *Platypoecilus maculatus* has the XY = male, XX = female type of sex determination. This fact now stands as well demonstrated as the WZ = female, ZZ = male system in the "domesticated" stocks of the same species.

The *Sb* Gene in Domesticated Stocks

After failing to capture another black-bottom platyfish in Mexico in 1939, we found as many of them as we wished to buy at a pet shop in New York. Similar purchases could probably have been made in any city in this country having a shop devoted to tropical aquarium fishes. A pair of black-bottoms was chosen at random from a lot shipped from a breeder in Florida. The purchased male black-bottom was as heavily pigmented, and in the same places, as its original wild 1932 progenitor. Female black-bottoms had been developed during the "domestication process" but

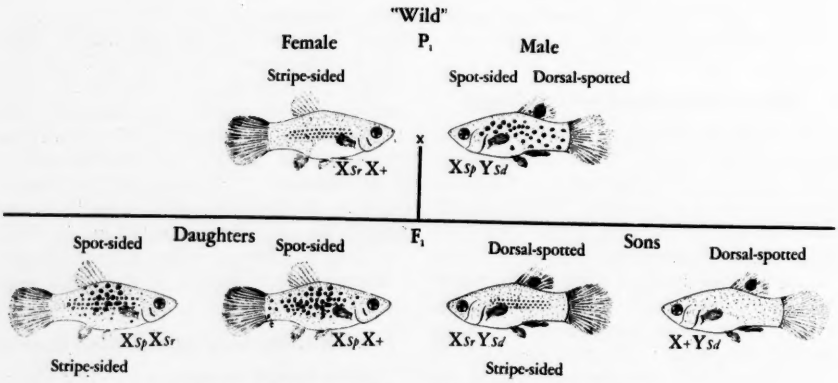
←**(Figure 11)**

This illustrates the breeding behavior of a normal, red, spotted female when crossed with a double recessive, gold, male. It shows definite criss-cross inheritance of two sex-linked genes *R* and S_p in F_1. A single exception occurred: a red, spotted female. This individual's appearance is accounted for by crossing over in the sex chromosomes of the P_1 female, resulting in transfer of the genes *R* and S_p from the Z to the W chromosome.

The exceptional red, spotted F_1 female was backcrossed to a double recessive male. The results show a different sort of inheritance: the dominant genes *R* and *Sp* were transmitted from mother to daughter and their recessive alleles *r* and s_p from father to son. Again an exception appeared: a red, spotted male. It is accounted for by crossing over in the sex chromosomes of the F_1 exceptional female, resulting in the transfer of the dominant genes *R* and S_p from the W back to the Z. (Reprinted from Fraser and Gordon, *Genetics*, 1929.)

On the basis of Castle's suggestion that YY = maleness and XY = femaleness (see page 318), the following may be substituted for the symbols used in the original plates:

♀		♂
(X)++/(Y)*SpR*	P_1 ×	(Y)++/(Y)++
	F_1	
43 (X)++/(Y)++		41 (Y)++/(Y)*SpR*
1 (X)*SpR*/(Y)++	×	(Y)++/(Y)++
	F_1 of Back-cross	
15 (X)*SpR*/(Y)++		17 (Y)++/(Y)++
		1 (Y)++/(Y)*SpR*



THE BEHAVIOR OF THREE "WILD" GENES

Figure 12

In 1939 a new stock of the platyfish (*P. maculatus*) was obtained from the Rio Jamapa, Veracruz, Mexico. This figure shows the genetic behavior of three sex linked "wild" genes *Sr*, *Sp* and *Sd*. The *Sd* gene is transmitted from father to son only. The *Sp* gene is transmitted from father to daughters only. The *Sr* gene is transmitted from the mother to both sons and daughters. The genetic behavior of these patterns may clearly be explained on the assumption that XY equals maleness and XX equals femaleness.

they were not quite as black as the males.

The genetic behavior of the "domesticated" black-bottom pair is illustrated in Figure 13. The strain is not true-breeding; all the sons and half of the daughters had the *Sb* gene; the remainder had the recessive +, or normal pattern. This experiment suggested the old "domesticated" sex-determining system, i.e. WZ = female, ZZ = male. A test of black-bottom females with recessive males, as illustrated in Figure 14, confirmed this hypothesis. The results were conclusive, for this mating produced only black-bottom sons and only normally colored daughters — the typical criss-cross behavior described by Bellamy, Gordon, Fraser and Gordon, and Kosswig for the "domesticated" platyfish. (In the experiment illustrated by Figure 14, the recessive male was of the "wild" stock, which is now known definitely to have the XY chromosomes. Thus the black-bottom male offspring were presumably of two genotypes, (Z)*Sb*/(X)+ and (Z)*Sb*/(Y)+, while the recessive female offspring were presumably (X)+/(W)+ and (Y)+/(W)+. The sex of these various sex-chromosome combinations among the F_1 may be noted for future reference.)

In another experiment a domesticated black-bottom female having the spotted (*Sp*) gene in addition to *Sb*: (Z)*Sb*/(W)*Sp*, was mated with a recessive wild male: (X)+/(Y)+, as illustrated by Figure 15. Again, the female offspring may be represented by XW and YW and the male offspring by ZX and ZY. Evidence that both gametes produced by the female (Z)*Sb* and (W)*Sp* were functional is shown by the presence of *Sb* sons and *Sp* daughters. Evidence that both gametes produced by the male, X and Y, are also functional, is given in the next experiment and illustrated by Figure 16.

The results from mating black-bottom females (*Sb*) with recessive males (+), are typical of criss-cross inheritance according to the ZW-female sex-determining system and are characteristic of "domesticated" platyfish.

What apparently happened, sometime between 1932 and 1939, was that the *Sb* gene, which had at one time followed the XY = male pattern of genetic be-

havior, now was following the WZ = female type.

Father to Son, Y = Z

Assuming the above to be true, then it would appear that if a "wild" female with homozygous sex chromosomes (XX) were to be mated with a "domesticated" male also having homozygous sex chromosomes (ZZ), all the offspring of such a mating should be uniform with respect to their chromosomes (XZ); on this basis all the offspring should be of one sex. A number of such matings were set up, and the results were indeed as expected — all of them were of one sex which proved to be male. The fact that they were all male rather than all female is consistent with the results obtained in the experiment illustrated in Figures 14 and 15 in which ZX fish were presumed to be males.

Figure 16 illustrates a mating between a "domesticated" male and a "wild" female in which the male parent was a black-bottom and spotted combination, *Sb/Sp*, while the female parent was a normal "wild" female, ++. Fifty per cent of the offspring were black-bottom (*Sb*/+), while the remaining fifty per cent were spotted (*Sp*/+). Both *Sb*/+ and *Sp*/+ offspring were males. The results show that unisexuality is not attained by the disfunction of one type of the two kinds of male gametes, for both types are represented in the offspring.

When one of the black-bottom male "domesticated-wild" hybrids (Z)*Sb*/(X)+ was mated back to a "wild" female of a spotted variety (X)*Sp*/(X)+ as indicated in Figure 17 all the sons were black-bottomed (*Sb*) while all of the daughters were recessive (+). The spotted gene (*Sp*) of the "wild" mother was transmitted to one-half of her sons and daughters.

When one of the F_1 males, (Z)*Sb*/(X)+, was backcrossed to a "wild" female, (X)+/(X)+, the results (see Figure 17) were as follows: the sons were like their father, (Z)*Sb*/(X)—, and the daughters were like their mother, (X)+/(X)+. When these offspring were mated to each other, the results were identical, in that generation and again in the next. The *Sb* gene was repeatedly passed along from father to son—through the Z chromosome.

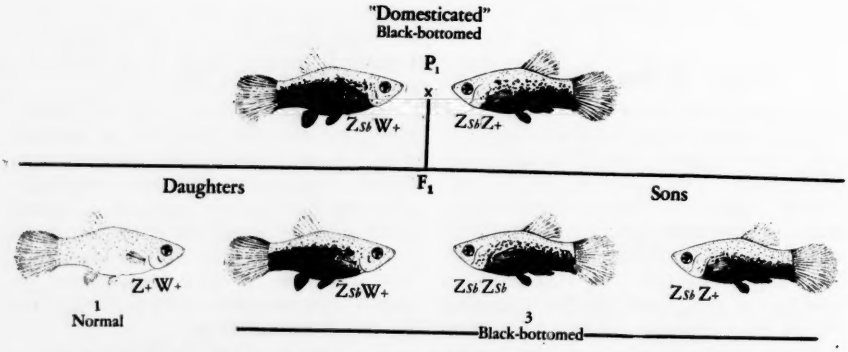
The "father-to-son" type of inheritance for the *Sb* gene has a familiar ring. It was exactly this type of sex-linked inheritance that was originally discovered in "wild" stocks of *P. maculatus* with the employment of the black-bottom gene. In the original black-bottom male, the *Sb* gene was carried by the Y chromosome—now it is carried by the Z chromosome.

The feature about the behavior of the *Sb* gene is this: that if the black-bottom male, regardless of whether *Sb* is associated with the Y or the Z chromosome, were returned to its wild associates from the rivers of Mexico, the character of the father would appear only in his sons.

How Has "Domestication" Come About?

What is it in the "domesticating process" that has brought about the change in the sex-determining mechanism of the wild *P. maculatus* from the XY = male, XX = female to the WZ = female, ZZ = male type? The answer to this question still escapes us. One suggestion may deserve consideration: the early platyfish which made up the preponderant group of aquarium-reared stocks originally may have come from a wild population in which the WZ system operates in nature. Since we have already checked some of the platyfish from the Rio Papaloapan and from the Rio Jamapa, and these populations have the XY system, the only other river systems from which they may have been originally taken are the Rio Coatzacoalcos or the Rio Usumacinta. In another paper dealing with speciation problems, Gordon[21] has suggested that the Rio Coatzaocalcos was the likely source. It would indeed be remarkable if the Rio Coatzacoalcos population proved to be of the WZ type. The genetic analysis of a sample of the population of this river might aid us in the solution of this problem.

The break-up of the rigid "father-to-



THE GENETIC BEHAVIOR OF THE BLACK-BOTTOM GENE AFTER THE "DOMESTICATION" PROCESS DURING 1933 TO 1940

Figure 13

Although over 8,000 wild platyfish were caught and examined carefully in the 1939 expedition, none with the black-bottom pattern was found among them. Yet one could get any number of "black-bottomed platies" at many tropical pet-fish shops in the U. S.: all of them are descendants of the one male caught and bred in 1932. All the new black-bottom platies now represent the cultivated stock of the strain. When interbred the genetic behavior pattern of the purchased pair resembled the "domesticated" type, i.e., ZZ equals maleness, ZW equals femaleness.

On the basis of Castle's suggestion that YY = maleness and **XY** = femaleness, the following symbols may be used to represent the above mating:

$$P_1 \quad (Y)Sb/(\mathbf{X})+ \;(♀) \times (Y)Sb/(Y)+ \;(♂)$$

$$F_1$$

(Y)+/(**X**)+, Normal ♀	(Y)*Sb*/(**X**)+, Black-bottom ♀	(Y)*Sb*/(Y)+, Black-bottom ♂	(Y)*Sb*/(Y)*Sb*. Black-bottom ♂.

son" type of inheritance, or the "mother-to-daughter" type of inheritance, is easily explained on the basis of the work of Gordon,[14] Fraser and Gordon[12] and Gordon.[17] There it was proved that the W and Z chromosomes in the domesticated stocks have a crossover rate of about one per cent. Unpublished data[23] show a slightly lower rate for crossing over of the X and Y chromosomes in wild stocks. Thus, domesticated female platyfish with the W-borne dominant genes, (W)*Sp*/(Z)+, in matings with homozygous recessive males, (Z)+/(Z)+, ordinarily produce spotted daughters and unspotted sons, but occasionally they produce a spotted son of the genotype (Z)*Sp*/(Z)+. Similarly, a wild spotted-dorsal male (X)+/(Y)*Sd* when mated to a wild normal female, (X)+/(X)+, will produce an occasional spotted dorsal female, (X)+/(X)*Sd*.[23]

These crossovers are not capable of changing the sex-determining mechanism from the wild XY-male to the domesticated WZ-female system. Nor do I believe the change-over is due to the method described in *Lebistes* by Winge,[33] who suggested that a pair of autosomes may take over the function of sex-determining chromosomes after the original sex chromosomes have been "neutralized" by crossing over.

Hybridization a Factor

One feature is involved in the *Platypoecilus* story which does not exist in *Lebistes*. It is the factor of species hybridization with *Xiphophorus hellerii*. Within a year after the swordtail was introduced into the aquaria of fish-fan-

ciers in 1910, hybrids between it and the platyfish were reported. The evaluation of the influence upon sex-determination of "wild" *Xiphophorus* chromosomes in company with those of *Platypoecilus* has not yet been thoroughly investigated, but the following example may illustrate the influence of hybridization.

When a spotted-dorsal and stripe-sided wild *P. maculatus* male (X)*Sr*/(Y)*Sd* was mated to a wild *X. hellerii* female, presumably (X′)+/(X′)+, the results were as follows:

50% = (X′)+/(X)*Sr*, striped-sided hybrids; these were all females and fertile.

50% = (X′)+/(Y)*Sd*, spotted-dorsal hybrids; these formed three groups:

a. about 5% were fertile males.

b. about 2% were fertile females.

c. about 92% were sexually indifferent. Some of group (c) had the appearance of males, most had the appearance of females; all of them were sterile.

Thus the association of the X chromosome of the platyfish was completely compatible with the X′ chromosome of the swordtail, but the Y platyfish chromosome was rarely compatible with X′.

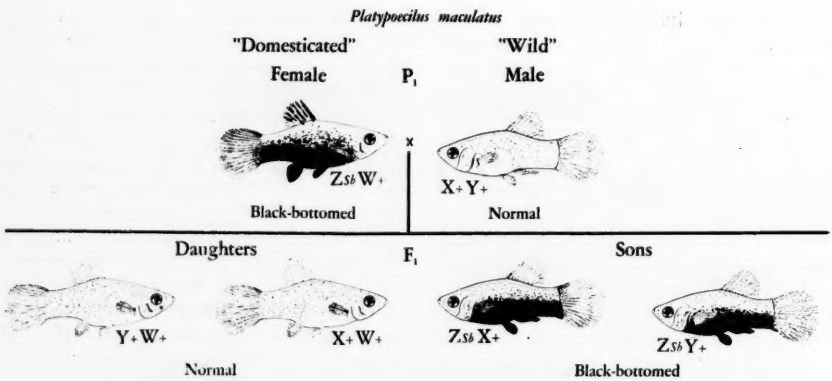
This work is progressing by mating a rare fertile F_1 platyfish-swordtail hybrid female with one of its slightly less rare fertile brothers. This mating may be expressed as follows: (X′)+/(Y)*Sd* × (X′)+/(Y)*Sd*, in which X′ represents a *Xiphophorus hellerii* chromosome and Y, a *Platypoecilus maculatus* sex chromosome. From this mating one might expect to get some (Y)*Sd*/(Y)*Sd* offspring which ought to be homozygous males. The next step will be to standardize females with the chromosomal constitution of (X′)+/(Y)*Sd*. This then would be equivalent to ZZ males and WZ females characteristic of the domesticated platyfish stocks.

It is indeed remarkable that when once the domesticated stocks of platyfish were established the WZ sex-determining mechanism was found to be stabilized in all the stocks tested. This may, perhaps, be accounted for by the fact that the earliest importations of the wild Mexican platyfish and swordtails were made into Germany in 1907-1909 according to the history of these domesticated fishes worked out by Gordon.[16] Hybrids between the two species were reported in 1910 and it is doubtful if pure stocks of either species were maintained long in the hands of the commercial tropical fish breeders. Fish culturists in the United States got their first platyfish and swordtails, not from Mexico, but from Germany; thus all the domesticated stocks of these fishes probably had a common origin.

Sex-Reversal

Only recently, after 20 years of genetic work with domesticated platyfish has the first case of complete and functional sex-reversal been reported in this stock. Breider[6] described a WZ fish which was expected to be a female on the basis of its phenotype but which turned out to be a functional male. He mated this presumed WZ male with a normal WZ female and obtained 51 female to 13 male offspring. By their phenotypes, he found that the sex ratio was as follows: 1 WW ♀ : 2 WZ ♀ : 1 ZZ ♂, three females to one male. Similarly, Gordon[23] reported a transformed wild stock platyfish, XX ♂ female that turned out to be a functional male. When this XX male was mated to a normal wild, XX female, all their 154 offspring were females. As in Breider's case of complete and functional sex reversal, the sex chromosomes retained their individual potentialities for sex determination after a temporary lapse.

In what seems to be an even more remarkable example of the individuality of the various sex chromosomes as they now appear in both the domesticated and wild stocks, the author will cite the preliminary results obtained by mating a domesticated-wild platyfish hybrid female of the constitution, (W)*Sp*/(X)+. This kind of female was one obtained in a mating shown in Figure 15, and it was crossed with a wild male, (X)+/(Y)*Sr*. The spotted offspring were all



"DOMESTICATED" FEMALE MATED WITH A "WILD" MALE

Figure 14

When the "domesticated" black-bottomed platy female was mated to a "wild" male, criss-cross inheritance was displayed, the character of the mother reappearing only in her sons. As a result of mating a ZW female with an XY male, the following new formulae for the sexes are derived: YW and XW are apparently female while ZX and ZY are apparently male.

On the basis of Castle's suggestion that YY = maleness and **XY** = femaleness in the WZ system, the following symbols may be used to represent the above mating.

$$P_1 \quad \text{♀ } (Y)Sb/(\mathbf{X})+ \times \text{♂ } (Y)+/(Y)+$$

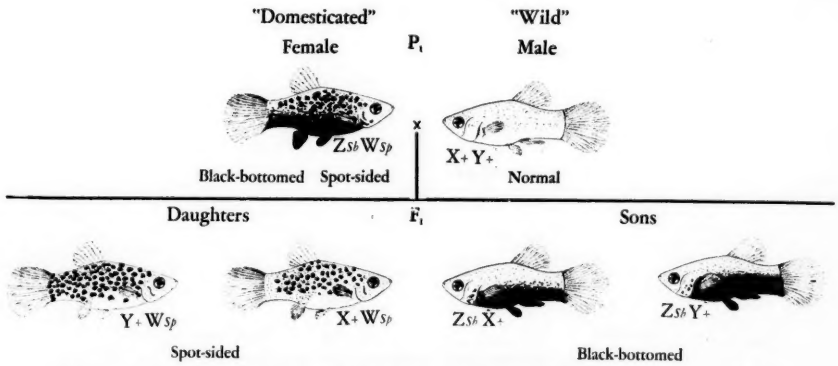
$$F_1 \quad (Y)+(\mathbf{X})+, \quad (Y)+/(\mathbf{X})+, \quad (Y)Sb/(Y)+, \quad (Y)Sb/(Y)+.$$

females, presumably (W)*Sp*/(X)+ and (W)*Sp*/(Y)*Sr*. But only half of the non-spotted offspring were male, presumably (X)+/(Y)*Sr*; the other half of the non-spotted offspring were female, presumably (X)+/(X)+. Thus there were three females: WX, WY, XX, to one male: XY. The ratio of 3:1 was the same as obtained by Breider but the method used, and the results obtained were quite different.

Diverse Results and Harmonious Conclusions

The sex-determining mechanism has been studied in two other species of xiphophorine fishes, *Platypoecilus xiphidium* and *P. variatus*. These fish species were first taken alive from Mexican streams in 1931 and 1932. Kosswig[26] and Bellamy,[4] by crossing male *P. maculatus* with female *P. xiphidium* or *P. variatus* obtained only male hybrid offspring. They concluded that since the *P. maculatus* males they used were known to be homozygous ZZ, the *P. xiphidium* and *P. variatus* females were probably homozygous XX, too, in order to account for all male hybrids. Gordon[17] took exception to this conclusion, pointing out that in a presumably similar experiment he obtained both male and female hybrid offspring in equal numbers.[a] This mating was illustrated later in the *American Journal of Cancer* 34:556-557, figures 11 and 12, by Gordon and Smith,[24] which showed the *P. maculatus* black-bottom male parent, the *P. variatus* female parent and their black-bottom male hybrids and the normally colored female hybrids. At that time no clear explanation for these divergent results was suggested.

These diverse results and conclusions may now be harmonized. Kosswig and Bellamy used domesticated male *P. maculatus* with wild *P. xiphidium* or *P. variatus* while Gordon and Smith



BOTH GAMATES OF THE "DOMESTICATED" FEMALE ARE FUNCTIONAL

Figure 15

To check the function of each of the two female gametes, one containing Z and the other containing W, both sex chromosomes were "marked." Both are functional as may be seen in the offspring: half were black-bottom males while the other half were spotted females.

Using Castle's symbols of YY= maleness, **X**Y = femaleness in the "domesticated" platyfish, the following may be substituted for the symbols above:

$$P_1 \qquad \text{♀ } (Y)Sb/(\mathbf{X})Sp \times \text{♂ } (X)+/(Y)+$$

$$F_1 \qquad (X)+/(\mathbf{X})Sp, \quad (Y)+/(\mathbf{X})Sp \qquad (Y)Sb/(X)+, \quad (Y)Sb/(Y)+.$$

Spot-sided daughters — Black-bottom sons

used the "wild" XY *P. maculatus* with a "wild" *P. variatus* female. Now all the facts fall into place properly by the simple suggestion which Gordon[19] has made that all three "wild" platyfish species have the XY-male type of sex determination while the "domesticated" *P. maculatus* has the WZ = female type.

Gordon[17] suggested that the type of sex-determining systems in P. *xiphidium* and in *P. variatus* might be more conclusively evaluated by utilizing the parallel sex-linked factors within natural populations of these species. Both have the spotted variety gene *Sp*. By their use in intervarietal matings in pure wild *P. xiphidium* and in pure wild *P. variatus* we are now prepared to say on the basis of adequate, but unpublished, data that the sex-determining system in each is XY equals male, XX equals female.

The type of sex-determining mechanism in the fourth species of the genus, *P. couchianus*, cannot be solved by similar methods for its spotted pattern is not quite comparable with those of its relatives. When an $(X)Sp/(Y)+$ *P. variatus* is mated with a presumably $(X)+/(X)+$ *P. couchianus* the male hybrids are unspotted $(X)+/(Y)+$, while the female hybrids are spotted $(X)Sp/(X)+$. When the reciprocal cross is made: *P. variatus* female $(X)Sp/(X)+$ mated with a *P. couchianus* male, presumably $(X)+/(Y)+$, there are spotted and unspotted males, spotted and unspotted females. If a spotted *variatus-couchianus* hybrid male is mated to an unspotted female then the male offspring are unspotted, while the female offspring are spotted. Thus *P. couchianus* appears to have the XY mechanism, too.

In his discussion of the opposing types of sex determination in the differing species of *Platypoecilus*, Castle[8] suggested that YY be used instead of ZZ; and XY be used rather than WZ for the

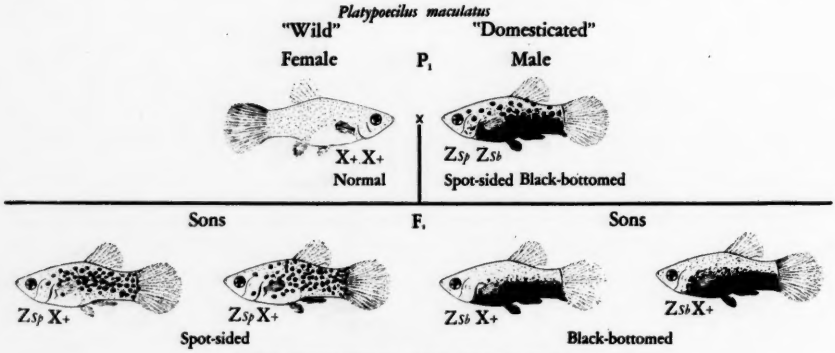


Figure 16

If the above reasoning is correct and the heterogametic chromosome formula ZW represents a "domesticated" platyfish female while, at the same time, the heterogametic chromosome formula XY represents a "wild" male of the same species, then their corollaries must also be true: the homozygous formula ZZ must represent the male "domesticated" platy and the homozygous chromosome formula XX must represent the female "wild" platy. As a consequence if a "wild" female were mated with a "domesticated" male, all their offspring should be of one sex for all of them would have the same sex chromosome mechanism, ZX. Furthermore, since from matings illustrated in Figures 14 and 15 we have determined that ZX equals maleness, we might predict that all the offspring would be males. This is exactly the result we obtained: all the offspring were male.

Using Castle's symbols of YY = maleness, **X**Y = femaleness in the "domesticated" platyfish, the following symbols may be substituted for those used above:

"Wild" ♀ (X)+/(X)+ × "Domesticated" ♂ (Y)*Sp*/(Y)*Sb*

F_1

(Y)*Sp*/(X)+, (Y)*Sp*/(X)+ Spot-sided sons

(Y)*Sb*/(X)+, (Y)*Sb*/(X)+. Black-bottom sons.

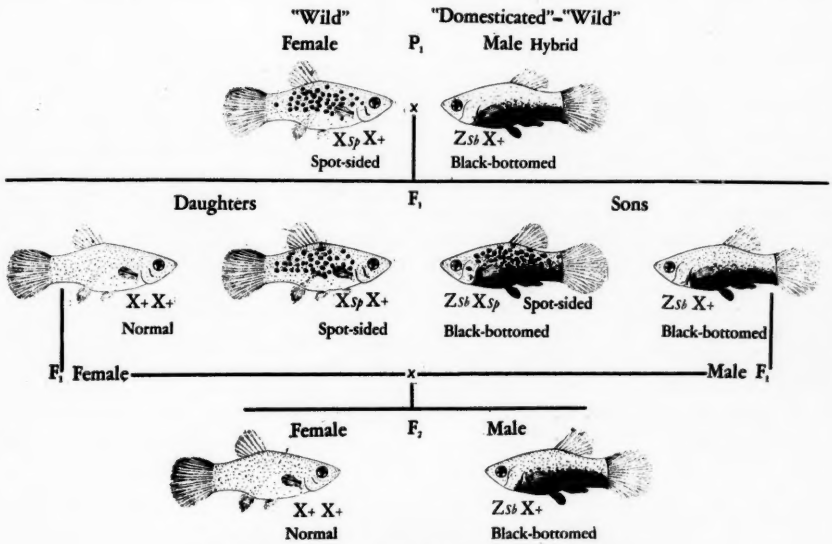
common aquarium-bred *P. maculatus*. For instance, in *P. variatus* XY expresses maleness while **X**Y expresses femaleness in *P. maculatus* ("domesticated" stock) or as he expresses it at another point:

	Female	Male
In Drosophila and man [*P. variatus*]	XX	X**Y**
In birds and moths [*P. maculatus*]	**X**Y	YY

The essential difference between the two systems, according to Castle, would seem to consist in a difference in the relative potency of X and Y, Y being dominant in the Drosophila system and X in the poultry system. In order to distinguish the two XY types, Castle uses bold face for the **X** in **X**Y of *P. maculatus* and bold type for **Y** in X**Y** of *P. variatus*. There is some merit in Dr. Castle's suggestion. The various combinations shown in the diagrams of this paper may be interpreted with these formulae, but it is suggested that the bold face type for the Y be altogether abandoned. The Y chromosome could readily replace the Z chromosome in all of our diagrams. The Y and Z apparently are homologous. But it would be advisable to maintain the bold faced **X** to represent our use of the **W** chromosome, for the **W** chromosome in present-day domesticated *P. maculatus* may represent a sex chromosome from *X. hellerii*.

Summary

1. The wild *Sb* gene for the black-bottom pattern, when it was originally tested with wild representatives of *Platy-*



FATHER TO SON INHERITANCE REPEATED

Figure 17

When a "Domesticated-Wild hybrid" black-bottom male from matings illustrated in Figures 14, 15 or 16 is tested with "Wild" females, the results are as shown here.

The wild female's genetic constitution is (X) *Sp*/(X)+ because it was spotted; the male hybrid's constitution is (Z)*Sb*/(X)+ because it was black-bottomed. From this mating, it may be seen that all the black-bottom offspring were male, and half of the males also were spot-sided. None of the female offspring was black-bottomed but half of them were spot-sided and half were normal.

When one of the black-bottom male offspring (Z)*Sb*/(X)+ was mated to one of its normal sisters (X)+/(X)+, the young of the next generation were like their immediate F_1 parents. And when the F_2 were mated together the black-bottomed character appeared only in the male offspring, just as it did in the F_1. Thus the *Sb* gene is again transmitted exclusively in the male line. But in this series of experiments the *Sb* is associated with the Z chromosome. It will be recalled that the *Sb* gene was associated with the Y chromosome (see Figure 9). While the genetic results are the same in the matings shown in Figures 9 and 17, apparently different chromosomes are involved.

If, as Castle suggests, the Y symbol is substituted for the Z, the "Domesticated-Wild" hybrid male's formula may be written (Y)*Sb*/(X)+ and since the "Wild" female to which it had been mated is (X)+/(X)*Sp*, the F_1 are as follows: (X)+/(X)+, (X)*Sp*/(X)+ which are daughters and (Y)*Sb*/(X)*Sp*, (Y)*Sb*/(X)+ are sons. When one of the F_1 recessive females, (X)+/(X)+ is mated to black bottom male, (Y)*Sb*/(X)+, the daughters are like their mother, (X)+/(X)+, while the sons are like their father, (Y)*Sb*/(X)+. The *Sb* gene is carried by the Y chromosome, just as it was originally in 1932.

poecilus maculatus, behaved as if it were carried by the Y chromosome and it demonstrated the father-to-son type of inheritance. After several years of breeding, presumably with domesticated stocks and possibly with *Xiphophorus hellerii,* the XY-male sex-determining reaction system of this strain was shifted to the well-established "domesticated" type known for aquarium-bred *P. maculatus,* in which WZ represents the female.

2. After the "domestication" process, the nature of which is not fully understood, the black-bottom gene *Sb* in males is usually carried by the Z chromosome as (Z)*Sb*/(Z)*Sb* or (Z)+/(Z)*Sb*. If the heterozygous "domesticated" male,

(Z)+/(Z)*Sb*, is mated with a "wild" recessive female, (X)+/(X)+, then all the F_1 are males, and half of them are normal, (Z)+(X)+, and half of them are black-bottom, (Z)*Sb*/(X)+.

3. If this black-bottom "domesticated — wild" male hybrid, (Z)*Sb*/(X)+, is backcrossed to a "wild" female, (X)+/(X)+, the phenotypes in pattern and sex are exactly like their parents, and this type of mating may be repeated with the same results again and again. The "father-to-son" type of inheritance shown by the (Z)*Sb*/(X)+ male repeats the behavior of the original black-bottom male (X)+/(Y)*Sb*. But now the Z chromosome behaves like the Y; and this suggests their homology.

4. The wild species of platyfishes, *Platypoecilus maculatus, variatus, xiphidium,* and probably *P. couchianus,* too, have similar types of genetic sex-determining mechanisms; XY equals maleness, XX equals femaleness. In the domesticated *P. maculatus,* ZZ equals maleness, ZW equals femaleness, or to use Castle's suggestion, YY = maleness; YX = femaleness.

5. The Z chromosome is probably homologous with the Y; but the W chromosome in domesticated stocks of *Platypoecilus maculatus* may represent a *Xiphophorus hellerii* sex chromosome. The substitution of a swordtail sex chromosome for a platyfish chromosome may have taken place as a result of frequent introgressive hybridization between these two species, under fish cultural practices.

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